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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/465,338	12/17/1999	Kenneth S. Albert	PT-1817	8786

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EXAMINER	
PULLIAM, AMY E	
ART UNIT	PAPER NUMBER
1615	27

DATE MAILED: 08/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/465,338	Applicant(s) ALBERT ET AL.	
	Examiner Amy E Pulliam	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-110* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) *48,49 and 60* is/are allowed.

6)☒ Claim(s) *1-47,50-59 and 61-110* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☒ Interview Summary (PTO-413) Paper No(s). *26* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Receipt of Papers

Receipt is acknowledged of the Extension of Time, the Preliminary Amendment F, and Request for Continued Examination, all received by the Office May 19, 2003.

Allowable Subject Matter

Claims 48, 49, and 60 are allowable.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-110 are provisionally rejected under the judicially created doctrine of double patenting over claims 1-66, 110, 112-119, and 122-132 of copending Application No. 09/567,451. This is a provisional double patenting rejection since the conflicting claims have not yet been patented.

The subject matter claimed in the instant application is fully disclosed in the referenced copending application and would be covered by any patent granted on that copending application

since the referenced copending application and the instant application are claiming common subject matter, as follows: Both applications disclose s controlled release Galenical p-reparation of pharmaceutically acceptable form of Diltiazem , suitable for evening dosing every 24 hours, comprising at least one bead comprising a core and at least one coating, with from about 120 mg to about 540 mg of active in the core, and wherein the coating comprises a hydrophilic polymer and/ or a lubricant, and a water insoluble polymer. Both Applications also claim a method of using the composition to treat a patient's hypertension and/ or angina. For these reasons, the two applications overlap in subject matter and necessitate a terminal disclaimer.

Furthermore, there is no apparent reason why applicant would be prevented from presenting claims corresponding to those of the instant application in the other copending application.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-15, 17, 19-37, 39, 43, and 63-78 are rejected under 35 U.S.C. 102(b) as being anticipated by EPA 856 313 to Geoghegan *et al.* ('313).

EPA '313 discloses a controlled absorption diltiazem pellet formulation for oral administration to control hypertension and angina comprising a core of diltiazem or a pharmaceutically acceptable salt thereof, and a multilayer membrane surrounding the core and

containing both a water insoluble and a water soluble polymer (abstract). EPA '313 further discloses that the formulation is preferred as a once-daily product to be administered before bedtime, and to be released at the following rates:

a. from 0 to 35% after 2 hours

b. from 4 to 45% after 4 hours

c. from 30 to 75% after 8 hours

d. from 60 to 95% after 13 hours

e. not less than 85% after 24 hours.

These release rates overlap those claimed by applicant in the instant application. Further, EPA '313 teaches that the water insoluble polymer can be replaced by a copolymer of acrylic and methacrylic acid esters (p 28, claim 10), and that the water soluble polymer can be HPMC (p 28, claim 7). EPA '313 also teaches that the core may comprise an organic acid, a lubricant (p 5, l 15-29), and other pharmaceutically acceptable components. In addition, throughout the examples, EPA '313 teaches varying amounts of active ingredient, including 120, 240, and 90 mg. Further, EPA '313 teaches tablet, pellet, and capsule formulations (exs. 8, 14, 21). Although EPA '313 does not disclose the exact release rates claimed by applicant, the ranges claimed fall within the range disclosed by EPA '313, and therefore anticipated by the reference.

Applicant's amendments and arguments have been fully considered but are not found to be persuasive. Applicant has amended the claims to include more specific limitations regarding the core and the coating. As the claim stands, the core requires the active agent and excipients, while the coating requires either a lubricant or a hydrophilic polymer and a water insoluble

swellable polymer. These limitations, however, are still anticipated by the cited reference. The reference teaches the use of a core and a coating, wherein the membrane coatings can comprise water soluble and water insoluble polymers. This directly reads on Applicant's claims.

The examiner spoke extensively with Marcelo Sarkis prior to issuing this office action. The examiner explained her position and why she felt the reference still read on the pending claims. Mr. Sarkis discussed that the critical feature of the invention is that the release of this formulation allows suitability for chronotherapeutic dosing. The examiner explained that this does not affect the patentability of a composition claim. Instead, if Applicant wishes to gain a patent on their composition, amendments must be made to the claims, incorporating any additional components, ratios, percentages, or other composition limitations which differentiate the cited art from the claimed composition. Unless differences in the actual composition can be shown, Applicant's can not be granted a composition claim. Mr. Sarkis also questioned the patentability of the method of use claims, as amended. The method claims are simply a method of using the composition of claim 1 by administering the composition to the patient in the evening. The cited reference, as stated above, teaches the claimed composition. Furthermore, the cited reference teaches administering the composition before bedtime, thus reading on the limitation to administer the composition in the evening. Therefore, as currently written, the examiner does not find the method claims to be patentable over the cited art.

The examiner expresses again that any differences between the prior art and the current claims must be inserted into the claim language. Functional language alone will not render a composition claim patentable. It is recommended that Applicant perform a side by side

comparison to determine any composition differences between the prior art and the instant claims, and that these differences be clearly set forth in the pending claims.

Mr. Sarkis and the examiner also discussed Applicant's use of a neutral copolymer as the water insoluble polymer. The examiner made several observations regarding this limitation. First, it is not found in the independent claims. Second, the reference broadly teaches the use of copolymers of acrylic and methacrylic acid esters (see claim 8 of the cited reference). Even if the working examples show charged copolymers, the claim do not require this limitation, and therefore there is nothing in the cited reference prohibiting the use a neutral copolymer as the water insoluble polymer. Last, Applicant has repeatedly stated that the main aspect of their invention is release of their formulation which allows for chronotherapeutic dosing. If the reason for this difference is the particular polymer used, the the examiner requests that the Applicant provide, in detailed form, why the use of a neutral copolymer instead of a charged copolymer would allow this distinction. Furthermore, it is necessary that this limitation be present in all independent claims.

For the above reasons, the examiner maintains her previously set forth rejections.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-47, 50-59, and 61-110 are rejected under 35 U.S.C. 103(a) as being unpatentable over EPA 856 313 to Geoghegan *et al.* ('313).

EPA '313 does not teach all of the specific amounts of Diltiazem present in the formulation, nor do they teach the specific wetting agent claimed by applicant. However, the formulation disclosed in EPA '313 does teach a varied range of the amount of active ingredient, as well as the presence of additional additives, such as lubricants. Further, the formulation also releases the drug at the same rate as that claimed by applicant, therefore, it appears that these limitations do not render any unexpected results. It is the position of the examiner that these are limitations which would be routinely determined by one of ordinary skill through minimal experimentation, as being suitable, absent the presentation of some unusual and/ or unexpected results. The results must be based on the specific limitations.

Furthermore, it is the position of the examiner that EP '313 teaches the generic concept of the invention, as well as the suggestion to manipulate the formulation to result in varying dissolution rates and Cmax values. One of ordinary skill in the art would have been motivated to manipulate the formulation based on the specifics of the desired formulation. The expected result would be a successful pharmaceutical formulation. Therefore, this invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Applicant's arguments have been fully considered but are not found persuasive. Applicant's arguments have been discussed in detail above. Again, the examiner repeats, if there is something different in applicant's formulation which makes is suitable for chronotherapeutic

release, while the cited art is not, it is recommended that these different components or ingredients be inserted into the claim language.

Claims 1-47, 50-59, 61, and 62 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 93/00093 to Deboeck *et al.* ('093). WO '093 discloses an extended release galenical form of Diltiazem or a pharmaceutically acceptable salt, with a wetting agent, coated with a microporous membrane comprising at least a water soluble polymer and a pharmaceutically acceptable adjuvant. WO '093 further teaches that the composition comprises beads containing between 120 and 480 mg of the active ingredient, with the wetting agent, and the beads are coated with the microporous membrane (p 19, claim 1). WO '093 further teaches that the water soluble polymer or copolymer can include HPMC and Eudragit (p 8, l 21-28). Further, WO '093 teaches that the following ingredients are included in the formulation: wetting agents such as fatty acid esters of saccharose (2-20%), microcrystalline cellulose (5-25%), polyvinylpyrrolidone (1-15%), titanium oxide, surfactants such as tween, antifoaming agents, magnesium stearate, and talc (see pages 8-10). These are the ingredients disclosed by applicant as being present in the formulation. WO '093 also teaches that the formulation is for once daily administration.

WO '093 does not teach the exact rates of release as claimed by applicant, nor do they discuss the rates of release after 8 hours, nor do they disclose all of the specific amounts of the above mentioned ingredients. However, WO '093 does teach overlapping rates of release to those claimed by applicant, and they do teach the same ingredients as claimed by applicant. It is the position of the examiner that the present application is not patentably distinct from WO '093,

as they contain the same ingredients, in the same formulation, with overlapping rates of release, even though WO '093 does not disclose the specific amounts of all the ingredients. It is the position of the examiner that the specific amounts of those ingredients which are not disclosed in WO '093 are limitations which would be routinely determined by one of ordinary skill in the art through minimal experimentation, absent the presentation of some unusual and/ or unexpected results. The results must be those that accrue from the specific limitations. Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to create a controlled release formulation of Diltiazem, based on the teachings of WO '093, and experiment with and vary the specific amounts of the ingredients, in order to achieve the desired rate of release.

Applicant argues that WO '093 does not teach the exact Cmax and Tmax as claimed by applicant. The examiner acknowledges this fact, and this is why the WO '093 reference is used as an obviousness reference, not an anticipation reference. It is the position of the examiner that because WO '093 contains the same ingredients in the same formulation, with overlapping release rates, applicant's invention is not patentably distinct from the prior art, therefore, this rejection is maintained.

Furthermore, applicant argues that the peak to trough variance for the WO '093 reference (which corresponds to Tiazac) is much larger than that of applicant's formulation. Applicant has provided evidence to reinforce this statement. However, the examiner respectfully disagrees as the data regarding Tiazac is concerning a 240 mg formulation, and the data regarding applicant's claimed formulation is based on a 300 mg capsule. Therefore, this comparison is not persuasive, and the rejection is maintained.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E Pulliam whose telephone number is 703-308-4710. The examiner can normally be reached on Mon-Thurs 7:30-5:00, Alternate Fri 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on 703-308-2927. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3592 for regular communications and 703-305-3592 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

A. Pulliam
Patent Examiner
Art Unit 1615
July 29, 2003

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Interview Summary	Application No. 09/465,338	Applicant(s) ALBERT ET AL.	
	Examiner Amy E Pulliam	Art Unit 1615	

All participants (applicant, applicant's representative, PTO personnel):

(1) *Amy E Pulliam*. (3)_____.

(2) *Marcelo Sarkis*. (4)_____.

Date of Interview: *29 July 2003*.

Type: a)☒ Telephonic b)☐ Video Conference
c)☐ Personal [copy given to: 1)☐ applicant 2)☐ applicant's representative]

Exhibit shown or demonstration conducted: d)☐ Yes e)☐ No.
If Yes, brief description: _____.

Claim(s) discussed: _____.

Identification of prior art discussed: _____.

Agreement with respect to the claims f)☒ was reached. g)☐ was not reached. h)☐ N/A.

Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: *See Continuation Sheet*.

(A fuller description, if necessary, and a copy of the amendments which the examiner agreed would render the claims allowable, if available, must be attached. Also, where no copy of the amendments that would render the claims allowable is available, a summary thereof must be attached.)

THE FORMAL WRITTEN REPLY TO THE LAST OFFICE ACTION MUST INCLUDE THE SUBSTANCE OF THE INTERVIEW. (See MPEP Section 713.04). If a reply to the last Office action has already been filed, APPLICANT IS GIVEN ONE MONTH FROM THIS INTERVIEW DATE, OR THE MAILING DATE OF THIS INTERVIEW SUMMARY FORM, WICHEVER IS LATER, TO FILE A STATEMENT OF THE SUBSTANCE OF THE INTERVIEW. See Summary of Record of Interview requirements on reverse side or on attached sheet.

Examiner Note: You must sign this form unless it is an Attachment to a signed Office action.

Examiner's signature, if required

Summary of Record of Interview Requirement

Manual of Patent Examining Procedure (MPEP), Section 713.04, Substance of Interview Must be Made of Record
A complete written statement as to the substance of any face-to-face, video conference, or telephone interview with regard to an application must be made of record in the application whether or not an agreement with the examiner was reached at the interview.

Title 37 Code of Federal Regulations (CFR) § 1.133 Interviews
Paragraph (b)
In every instance where reconsideration is requested in view of an interview with an examiner, a complete written statement of the reasons presented at the interview as warranting favorable action must be filed by the applicant. An interview does not remove the necessity for reply to Office action as specified in §§ 1.111, 1.135. (35 U.S.C. 132)

37 CFR §1.2 Business to be transacted in writing.
All business with the Patent or Trademark Office should be transacted in writing. The personal attendance of applicants or their attorneys or agents at the Patent and Trademark Office is unnecessary. The action of the Patent and Trademark Office will be based exclusively on the written record in the Office. No attention will be paid to any alleged oral promise, stipulation, or understanding in relation to which there is disagreement or doubt.

The action of the Patent and Trademark Office cannot be based exclusively on the written record in the Office if that record is itself incomplete through the failure to record the substance of interviews.

It is the responsibility of the applicant or the attorney or agent to make the substance of an interview of record in the application file, unless the examiner indicates he or she will do so. It is the examiner's responsibility to see that such a record is made and to correct material inaccuracies which bear directly on the question of patentability.

Examiners must complete an Interview Summary Form for each interview held where a matter of substance has been discussed during the interview by checking the appropriate boxes and filling in the blanks. Discussions regarding only procedural matters, directed solely to restriction requirements for which interview recordation is otherwise provided for in Section 812.01 of the Manual of Patent Examining Procedure, or pointing out typographical errors or unreadable script in Office actions or the like, are excluded from the interview recordation procedures below. Where the substance of an interview is completely recorded in an Examiners Amendment, no separate Interview Summary Record is required.

The Interview Summary Form shall be given an appropriate Paper No., placed in the right hand portion of the file, and listed on the "Contents" section of the file wrapper. In a personal interview, a duplicate of the Form is given to the applicant (or attorney or agent) at the conclusion of the interview. In the case of a telephone or video-conference interview, the copy is mailed to the applicant's correspondence address either with or prior to the next official communication. If additional correspondence from the examiner is not likely before an allowance or if other circumstances dictate, the Form should be mailed promptly after the interview rather than with the next official communication.

The Form provides for recordation of the following information:
- Application Number (Series Code and Serial Number)
- Name of applicant
- Name of examiner
- Date of interview
- Type of interview (telephonic, video-conference, or personal)
- Name of participant(s) (applicant, attorney or agent, examiner, other PTO personnel, etc.)
- An indication whether or not an exhibit was shown or a demonstration conducted
- An identification of the specific prior art discussed
- An indication whether an agreement was reached and if so, a description of the general nature of the agreement (may be by attachment of a copy of amendments or claims agreed as being allowable). Note: Agreement as to allowability is tentative and does not restrict further action by the examiner to the contrary.
- The signature of the examiner who conducted the interview (if Form is not an attachment to a signed Office action)

It is desirable that the examiner orally remind the applicant of his or her obligation to record the substance of the interview of each case. It should be noted, however, that the Interview Summary Form will not normally be considered a complete and proper recordation of the interview unless it includes, or is supplemented by the applicant or the examiner to include, all of the applicable items required below concerning the substance of the interview.

A complete and proper recordation of the substance of any interview should include at least the following applicable items:
1) A brief description of the nature of any exhibit shown or any demonstration conducted,
2) an identification of the claims discussed,
3) an identification of the specific prior art discussed,
4) an identification of the principal proposed amendments of a substantive nature discussed, unless these are already described on the Interview Summary Form completed by the Examiner,
5) a brief identification of the general thrust of the principal arguments presented to the examiner,
   (The identification of arguments need not be lengthy or elaborate. A verbatim or highly detailed description of the arguments is not required. The identification of the arguments is sufficient if the general nature or thrust of the principal arguments made to the examiner can be understood in the context of the application file. Of course, the applicant may desire to emphasize and fully describe those arguments which he or she feels were or might be persuasive to the examiner.)
6) a general indication of any other pertinent matters discussed, and
7) if appropriate, the general results or outcome of the interview unless already described in the Interview Summary Form completed by the examiner.

Examiners are expected to carefully review the applicant's record of the substance of an interview. If the record is not complete and accurate, the examiner will give the applicant an extendable one month time period to correct the record.

Examiner to Check for Accuracy

If the claims are allowable for other reasons of record, the examiner should send a letter setting forth the examiner's version of the statement attributed to him or her. If the record is complete and accurate, the examiner should place the indication, "Interview Record OK" on the paper recording the substance of the interview along with the date and the examiner's initials.

Continuation of Substance of Interview including description of the general nature of what was agreed to if an agreement was reached, or any other comments: The examinre and the attorney of record spoke extensively about the patentability of this application. The examiner explained that the present amendments to not appear to differentiate from the cited prior art, for the specific reasons discussed in the attached action. The examiner again exphasized that any differences betweeen the cited art composition and the pending application composition must be clearly set forth in the composition claims using additional composition components or amounts of ingredients. Such differences can not be expressed through functional language. Please see the attached action for further discussion..